Fascin, a novel target of beta-catenin-TCF signaling, is expressed at the invasive front of human colon cancer.

Abstract: Cancer cells become metastatic by acquiring a motile and invasive phenotype. This step requires remodeling of the actin cytoskeleton and the expression of exploratory, sensory organelles known as filopodia. Aberrant beta-catenin-TCF target gene activation plays a major role in colorectal cancer development. We identified fascin1, a key component of filopodia, as a target of beta-catenin-TCF signaling in colorectal cancer cells. Fascin1 mRNA and protein expression were increased in primary cancers in a stage-dependent manner. Fascin1 was exclusively localized at the invasive front of tumors also displaying nuclear beta-catenin. Forced expression of fascin1 in colorectal cancer cells increased their migration and invasion in cell cultures and caused cell dissemination and metastasis in vivo, whereas suppression of fascin1 expression by small interfering RNA reduces cell invasion. Although expression of fascin1 in primary tumors correlated with the presence of metastases, fascin1 was not expressed in metastases. Our studies show that fascin1 expression is tightly regulated during development of colon cancer metastases and is a novel target of beta-catenin-TCF signaling. We propose that transient up-regulation of fascin1 in colorectal cancer promotes the acquisition of migratory and
invasive phenotypes that lead to metastasis. Moreover, the expression of fascin1 is down-regulated when tumor cells reach their metastatic destination where migration ceases and proliferation is enhanced. Although metastasis to vital organs is often the cause of mortality, only limited success has been attained in developing effective therapeutics against metastatic disease. We propose that genes involved in cell migration and invasion, such as fascin1, could serve as novel targets for metastasis prevention.